disease might be segregated from patients with non-Alzheimer's dementia by the finding of elevated levels of A4 or β-peptide in the blood or cerebrospinal fluid—that is, a simple biochemical test could be used to confirm the presence of Alzheimer's disease. This is now done inferentially from clinical data and imaging studies, and the autopsy is used for definitive confirmation.

The A4 protein has been shown to be accumulated within lysosomes of certain neuronal populations in the brain, suggesting that proteolysis of the precursor with resultant deposition of the A4 or β-peptide within tissues may be a pivotal event in the neuronal degeneration that characterizes Alzheimer's disease both clinically and pathologically. In any event, research into possible mechanisms of processing of the A4 peptide into an insoluble form in the brain may lead to therapeutic strategies by which this processing can be engineered so that smaller amounts of microvascular and senile plaque amyloid are ultimately deposited within brain parenchyma. It remains an open question whether this will lead to stabilization or amelioration of the clinical signs and symptoms of Alzheimer's disease or Alzheimer's senile dementia.

This work was supported in part by the National Institutes of Health, Public Health Services grant NS 26312-03.

HARRY V. VINTERS, MD
Los Angeles, California

REFERENCES

Benowitz LI, Rodriguez W, Paskevich P, Mufson EJ, Schenk D, Neve RL: The amyloid precursor protein is concentrated in neuronal lysosomes in normal and Alzheimer disease subjects. Exp Neurol 1989; 106:237-250

Podlisny MB, Mammen AL, Schlossmacher MG, Palmert MR, Younkin SG, Selkoe DJ: Detection of soluble forms of the β-amyloid precursor protein in human plasma. Biochem Biophys Res Commun 1990; 167:1094-1101

Selkoe DJ: Deciphering Alzheimer's disease: The amyloid precursor protein yields new clues. Science 1990; 248:1058-1060

Vinters HV, Miller BL, Pardridge WM: Brain amyloid and Alzheimer disease. Ann Intern Med 1988; 109:41-54

Vinters HV, Secor DL, Pardridge WM, Gray F: Immunohistochemical study of cerebral amyloid angiopathy—III: Widespread Alzheimer A4 peptide in cerebral microvessel walls colocalizes with γ trace in patients with leukoencephalopathy. Ann Neurol 1990; 28:34-42

Stereotactic Brain Biopsy

THE MANAGEMENT OF MASS LESIONS of the brain continues to evolve with the increasing availability of stereotactic biopsy. Stereotactic biopsy is done through a small drill hole in the skull under local anesthesia and carries an extremely small risk of complications. The total time for obtaining a biopsy specimen is about two hours. Most patients come in for the procedure in the morning and leave the hospital after an overnight observation period. Stereotactic biopsy is capable of procuring tissue from virtually any location within the cranial cavity, including the third ventricle, hypothalamic region, brain stem, and posterior fossa. The availability of stereotactic biopsy allows the histologic diagnosis of any brain mass.

Basic mathematic principles are used to identify any point within the cranial cavity by means of three coordinates. The stereotactic instruments provide the three coordinates that guide the biopsy forceps to a target point determined on the radiologic image. With experience, representative material is procured in virtually all cases.

The pathologic interpretation is limited by the small size of the specimen, however. The accuracy of histologic diagnosis in experienced hands is about 90% overall. The use of smears is highly recommended as the primary means of making a diagnosis.

The accuracy and specificity of diagnosis are greatest for regionally homogeneous neoplastic lesions such as metastatic carcinoma, craniopharyngioma, oligodendroglioma, and malignant lymphoma. In these cases, the diagnosis depends only on the neurosurgeon obtaining tissue from the lesion and the pathologist making the correct diagnosis.

In regionally heterogeneous neoplasms such as astrocytomas and pineal germ cell neoplasms, the small size of the specimen creates theoretical problems. Here the diagnosis depends not only on obtaining abnormal material and the pathologic interpretation but also on regional differences within the neoplasm. Two solutions are available at stereotactic biopsy to overcome this problem. The first is to take several specimens from different target points in the lesion, increasing the tissue volume to provide a representative sample. This adds to the time and risk of the procedure but is an acceptable solution. The second is to interpret the biopsy in conjunction with full clinical and radiologic data to arrive at a clinicopathologic diagnosis. We use the latter method, and it has been our experience that a single specimen from an astrocytic neoplasm provides an accurate placement of the lesion in a three-tiered classification that is adequate for appropriate clinical management. The use of a single biopsy specimen in conjunction with tumor markers and radiologic features is adequate for most pineal germ cell neoplasms.

The lowest accuracy rate for stereotactic biopsy is attained when the biopsy specimen shows inflammation. Most of these will be nonneoplastic lesions. The rate of identifying a specific cause is low and requires careful handling of the tissue for immunohistochemistry (viral antigens), electron microscopy (viral particles), culture, and polymerase chain reaction (viral nucleic acid). Although a stereotactic biopsy specimen that shows inflammation is rarely from a neoplasm, we have had specimens interpreted as nonspecific inflammation turn out on a subsequent specimen to be malignant lymphoma, Hodgkin's disease, pineal germinoma, and anaplastic astrocytoma. It is prudent, therefore, to carefully evaluate inflammatory lesions diagnosed on stereotactic biopsy for the possibility of a neoplasm.

PARAKRAMA CHANDRASOMA, MD
Los Angeles, California

REFERENCES

Apuzzo ML, Chandrasoma PT, Cohen D, Zee CS, Zelman V: Computed imaging stereotaxy: Experience and perspective related to 500 procedures applied to brain masses. Neurosurgery 1987; 20:930-937

Chandrasoma PT, Apuzzo ML: Stereotactic Brain Biopsy. New York, NY, Igaku-Shoin, 1989

Chandrasoma PT, Smith MM, Apuzzo ML: Stereotactic brain biopsy in the diagnosis of brain masses: Comparison of results of biopsy and resected surgical specimen. Neurosurgery 1989; 24:160-165

Willems JGMS, Alva-Willems JM: Accuracy of cytologic diagnosis of central nervous system neoplasms in stereotactic biopsy. Acta Cytol 1984; 28:243-249

Micrometastases in Melanoma

THE FIVE-YEAR SURVIVAL RATE for patients with melanoma spread to the regional nodes, the first site of metastasis for most melanoma patients, varies from 20% to 50% according to the number of nodes that contain metastatic melanoma and the micrometer measured thickness of the primary tumor.